REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

Unity of Invention

The examiner has restricted the claims for unity of lack invention on the basis that Chiba reference anticipates the present invention. As discussed below, however, the Chiba reference does not disclose the present invention. Therefore, applicants respectfully request that the finding of lack of unity of invention be withdrawn and all of the claims be examined together.

Drawings

The Examiner has not yet indicated in the Office Action Summary that the formal drawings filed with the original application papers have been accepted. Acceptance of these drawings is respectfully requested in the next communication from the Examiner.

Priority Document

In the Office Action dated May 20, 2005, the Examiner did not check Box 12 of the Office Action Summary indicating "acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f). Accordingly, the Examiner in respectfully requested to check this box in the next communication from the PTO

Rejections Under 35 USC 112, First and Second Paragraph

Applicants traverse the examiner's findings for lack of enablement and written description of the following reasons.

The examiner stated that the disclosure is limited to a method of preparing a Saccharomyces cerevisiae mutant by disrupting MNN1, MNN4, and OCH1 genes normally present in S.cerevisiae with selection markers in claim 92 and transforming the resulting S.cerevisiae mutant with a specific polynucleotide isolated from Aspergillus saitoi encoding α-mannosidase I and a polynucleotide isolated from a rat encoding GnT-I (OA, page 11, line 3 from the bottom-page 12, line 3). Therefore, the examiner asserts the specification does not

support the broad scope of the claims, which encompass a method of preparing any yeast by disrupting any or all MNNI, MNN4, and OCHI genes using any methods and transforming the resulting mutant yeast with a polynucleotide encoding any α-mannosidase I and a polynucleotide encoding any GnT-I (OA, page 13, second paragraph).

With respect to yeasts, multiple genes having certain common functions are present across the multiple species of yeasts in general. For example, it was confirmed at the time of filing the present application that the OCH1 gene is present in Pichia pastoris as well as in Saccharomyces cerevisiae. (See Japanese Published Patent Application No. 09-003097). After filing the present application, it has been confirmed that the OCHI gene is also present in multiple other species of yeasts, such as Candida albicans (GenBank, AY064420) and Kluyveromyces lactis (GenBank, AJ42 8417).

The yeasts used for mutation in the method of the present invention possess an MNN1 gene having a function of adding mannose through α-1,3 linkage (see page 5, lines 4 to 5 of the specification), an MNN4 gene having a function of adding mannose-l-phosphate (page 5, lines 7 to 17 in the specification), and an OCH1 gene having a function of adding mannose through α-1,6 linkage (page 4, lines 4 to 6 from the bottom in the specification). The yeasts used in the present invention also incorporate yeasts wherein the above genes are initially present but are disrupted spontaneously (page 26, last paragraph, lines 1 to 3 in the specification).

Saccharomyces cerevisiae is only a representative example of yeasts having these features. Taking into account of the common technical knowledge at the time of filing of the present application, one of skill in the art would understand that Saccharoniyces cerevisiae is a working example and the present invention can be used in other yeasts. Therefore, applicants urge that the present invention covered is fully described and enabled by the example using Saccharomyces cerevisiae. That is, a person skilled in the art would be able to practice the present invention in other yeasts with undue burden.

In the same vein, applicants urge that the one of skill in the art would understand that the selection markers, such as the auxotrophic marker URA3 is only a representative example. It is common technical knowledge that any markers can be used for disrupting genes. This is supported by the description of the specification at page 27, third paragraph,

lines 1 to 4. In light of the teachings of the specification, applicants contend that the disruption of a gene would nof present an undue burden to one of skill in the art.

α-mannosidase has a function of specifically cleaving the α-1,2-linked side chain and producing free mannose (Abstract of Biochim. Biophys. Acta. Vol. 658, pp. 45-53, March 1981, attached as Exhibit I) and GnT-I has a function of converting high-mannose N-glycans to complex and hybrid N-glycans (page 234, left column, lines 26-29 of Proc. Natl. Acad. Sci. USA. Vol. 88, pp. 234-238, January 1991, attached as Exhibit II). Any kinds of α-mannosidase gene and GnT-I gene having the above features (functions) can be used in the present invention. A polynucleotide isolated from Aspergillus saitoi encoding α-mannosidase I and a polynucleotide isolated from a rat encoding GnT-1 are only representatives of genes having these features. Therefore, the invention present is fully enabled by the examples using α-mannosidase I derived from Aspergillus saitoi (page 41, Example 4) and rat GnT-I (page 43, Example 5).

Therefore, applicants respectfully request withdrawal of the rejections for lack of enablement and written description.

Claim Rejections-35 USC 102

The Examiner asserts that Chiba et al. discloses a method of preparing a mutant yeast that produces the glycoprotein of' formula (IV) by transforming a S.cerevisiae comprising Δ mnn1 Δ mnn4 Δ och1 triple mutant with a polynucleotide encoding an A.saitoi α-mannosidase I and a polynucleotide encoding GnT-I. Thus, the examiner rejects claims 88 and 92-94 under 35 USC 102 (b) as being anticipated by Chiba et al.

Applicants contend that this rejection is improper because the present invention represents the first time that a glycoprotein having a hybrid-type sugar chain represented by formula (IV) has been successfully produced in vivo. In Chiba et al., introduction of the GnT-1 gene into host cells is not actually conducted. In fact, there is a description that "...to make hybrid- and complex-type sugar chains in yeast cells, co-expression of GnT-I and α-1,2-mannnosiclase (α-mannnosidase I) is required and is an object of our further research" See page 26303, right column, times 1 to 3 from the bottom. Therefore thre Chiba reference is merely a suggestion for further research and does not anticipate the present invention.

The present application, with respect to a yeast mutant (TIY19pYOMG4), wherein the MNN1 gene, the MNN4 gene, and the OCH1 gene are disrupted and into which the α-mannnosidase I gene and the GnT-I gene are introduced, it is actually confirmed that the sugar chain of cell surface mannan-protein of the yeast is a hybrid-type sugar chain represented by formula (IV).

Such result obtained in the present application is not disclosed in Chiba et al. Therefore, the present application should not be rejected as being anticipated by Chiba et al. under 35 USC 102(a).

Conclusion

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorize payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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By _____

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